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EXAMINER	
GOLDBERG, JEANINE ANNE	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 08/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/621,009	BROWN, BOB D.	
	Examiner	Art Unit	
	Jeanine A. Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17, 50-74* is/are pending in the application.

4a) Of the above claim(s) *71-74* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17 and 50-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the papers filed June 28, 2005. Currently, claims 1-17, 50-74 are pending. Claims 71-74 have been withdrawn as drawn to non-elected subject matter.

Election/Restrictions

2. Applicant's election without traverse of Group I, claims 1-17, 50-70 in the paper filed June 28, 2005 is acknowledged.

Claims 71-74 are drawn to a method for amplifying which is the subject matter of Group II of the election requirement. Claims 71-74 are withdrawn in view of the restriction requirement and election.

Priority

3. This application claims priority to 09/932,129, filed August 16, 2001, PCT US00/09230, filed April 7, 2000 and provisional application 60/128,378, filed April 8, 1999.

If applicant desires benefit of a previously filed application under 35 U.S.C. 120, specific reference to the earlier filed application must be made in the instant application. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. This should appear as the first sentence(s) of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet. The

status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless

previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Specification

4. The amendment filed 6/28/05 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows.

The amendment to the specification proposes to add three new paragraphs which do not appear to be part of the original disclosure. The response fails to point to any particular support for the added paragraphs.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1, 4-7, 9-10, 13-16, 50, 53-56, 58-59, 62-65 are rejected under 35 U.S.C. 102(b) as being anticipated by Hogan et al. (US Pat. 5,424,413, June 13, 1995).

Hogan et al (herein referred to as Hogan) teaches branched nucleic acid probes. Hogan teaches nucleic acid probes having at least on nucleic acid strand which has at least two separate target specific regions that hybridize to a target nucleic acid sequence, and at least two distinct arm regions that do not hybridize with the target nucleic acid but possess complementary regions that are capable of hybridizing to one another. Hogan teaches the probes form branched nucleic acid structures upon interaction with and hybridization to a target nucleic acid. The probes can be modified DNA or RNA including inosine or modified internucleotide linkages (e.g., phosphorothioate or methyl phosphonate)(col. 6, lines 10-20)(limitations of Claims 5-6). Hogan teaches the probe regions are between 8-50 nucleotides in length (col. 8, lines 25-30)(limitations of Claim 7). As described in Example 9, DNA/RNA polymerase extension is described. Figure 15C illustrates the arm regions are designed so as to create site for extension by a polymerase. The filled-in region can be detected by detecting extended primer, for example. Alternatively, as illustrated in Figure 15D fill-in with a polymerase creates an active T7 RNA promoter site (col. 21). The template strand, the anchor, comprises a nucleic acid chemistry which has a 3'-end which is not capable of priming nucleic acid synthesis. Further, the primer strand, the primer, has a

nucleic acid chemistry that is a substrate for DNA polymerase. The anchor and the primer comprise a region of complementary nucleotides which form a stem structure (limitations of Claim 1). As seen in Figure 15C, the Template strand extends further than the primer strand. Further, a universal primer may have any sequence, thus, the stem has a sequence which is complementary to a universal primer.

6. Claims 1-2, 4-17, 50-52, 54-70 are rejected under 35 U.S.C. 102(e) as being anticipated by Ulanovsky et al. (US Pat. 6,197,556 B1, filed May 7, 1997).

Ulanovsky et al. (herein referred to as Ulanovsky) teaches modular branched primers. The stem portions of branched primers are constant and bind portions of variable modules together to give specificity to the initial priming (extension) yet allow amplification using conventional primers to proceed (col. 2, lines 23-26). As seen in Figure 2(1)- Figure 2(4), a pair of branched primers are extended in both the forward and reverse directions followed by a pair of unbranched primers. A branched pair of primers is comprised of a front module, a front arm, a back module and a back arm (Figure 4). The two oligonucleotide modules (font and back) also have an "arm segment" which is complementary to a nucleotide sequence site in a template (col.2, lines 43-45). Ulanovsky teaches that "front" refers to the 3' extending (downstream) sequence and "back" refers to the 5' end (upstream). The stem segments are complements of each other and anneal to form the stem of the branched primer (col. 2, lines 30-41). The arm segments is complementary to a nucleotide sequence site in a template to be amplified (col. 2, lines 43-50). The first initial extension strand is annealed to a reverse primer which may be either branched or not to form a second

initial extension strand (col. 2, lines 50-55). Then the products are amplified by using amplification primers that include a reverse primer and/or at least one primer homologous to the stem sequence of the first and/or second branched primer (col. 2, lines 55-60). The strand resulting from the extension of the first initial primer is used as a template and the two PCR primers are a reverse primer and the front module of the first initial primer (or a universal primer homologous to the stem of the first module)(col. 9, lines 45-55)(limitations of Claim 8, 10, 17).

Ulanovsky teaches a nucleotide connecting the variable segment with the rest of the oligonucleotide (linkers) can have any base, but preferably such modification, as Inosine or Deoxynebularin (both available from Glen Research Corp., VA, USA), which have approximately equal energy of base-pairing with all four normal bases. This linker between the arm and stem can also be just a chain of atoms (linker) with no base at all, like "AminoModifier II", available for DNA synthesis from Clontech, CA, USA. The purpose of the weak base-pairing of the linker is to make the annealing site more unique. Otherwise, that is if the linker has one of the four normal bases without weakened base-pairing, it can generate undesirable extra binding sites together with nucleotides adjacent to it (limitations of Claim 2, 11).

Ulanovsky also teaches that the arm of each oligonucleotide module sequence preferably contains at least one artificial base to reduce steric hindrance that may be caused by proximity of the stem to the extension point and/or to enhance the annealing stability. These base modifications can be either of bases or backbones in modular primer that improve the stability of annealing, such as PNA, methyl phosphonate, 5-

methylcytidine and 2-aminoadenosine (col. 2, lines 60-67; col 13, lines 17-20)(limitations of Claim 5, 6, 14, 15). As seen in the example, the PCR amplification is demonstrated using four branched DNA primers (col. 18)(limitations of Claim 67-68). At least one of the amplification primers is optionally protruding by one or more bases immediately downstream of the 3'-end. This protrusion increases the sequence-specificity of the amplification (col. 4, lines 38-42)(limitations of Claim 4). The protruding amplification primers may include artificial bases, which reduce the number of possible sequences of these primer that need to be made (col. 4, lines 40-43). Ulanovsky teaches using a thermostable polymers for the initial extension such as ampliTaq and Stoffel fragment (col. 2, lines 55-65). Figure 4 illustrates the first target binding region comprising at least 6 nucleotides, namely 6 nucleotides (limitations of Claim 7, 16). Ulanovsky teaches the present invention also includes a library that is a collection of modular oligonucleotides in separate receptacles (i.e. kit)(col. 4, lines 59-67)(limitations of Claims 50-52, 54-70).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 3, 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ulanovsky et al. (US Pat. 6,197,556 B1, filed May 7, 1997) as applied to Claims 30, 35, 47 above and further in view of Stefano et al. (US Pat. 6,287,772, filed April 29, 1998).

Ulanovsky does not specifically teach using a flexible linker of polyethylene glycol, polyethylene, polypropylene, polyesters, between the first stem region and the target binding region.

However, Stefano teaches in Figure 2A a linker between the first stem region and the target binding region. Stefano teaches PNA is a polyamide (col. 7, lines 14-15). Moreover Stefano teaches spacers are used to minimize the adverse effects that bulky labeling reagents might have in hybridization properties of non-nucleic acid probes (col. 7, lines 30-40). Linkers typically induce flexibility and randomness into the probe or otherwise link two or more nucleobase sequences of a probe or component polymer (col. 7, lines 30-40). Stefano teaches that many linker/spacer moieties are known in the art and provides a variety (col. 7).

Therefore, it would have been prima facie obvious to one of ordinary skill at the time the invention was made to have added a spacer/linker, as taught by Stefano, into the primer modules of Ulanovsky for the expected benefit taught by Stefano. Stefano teaches that spacers/linkers are used to minimize adverse effects, increase flexibility and randomness. Thus, the ordinary artisan would have been motivated to incorporated a spacer/linker into the branched probe of Ulanovsky between the arm and the target region to minimize adverse effects, and increase flexibility.

Conclusion

8. No claims allowable over the art.

9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

A) Egholm et al. (US Pat. 6,451,588, September 2002) teaches multipartite high-affinity nucleic acid probes which comprise a flexible linker (see Figure 1A).

B) Weston et al. (US Pat. 6,391,593, May 21, 2002) teaches methods of detecting nucleic acid sequences using modified nucleic acid probes (see Figure 1).

C) Kandimalla et al. (US Pat. 6,372,427, April 2002) teaches cooperative oligonucleotides.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (571) 272-0743. The examiner can normally be reached Monday-Friday from 7:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272- 0745.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Central Fax Number for official correspondence is (571) 273-8300.

Jeanine Goldberg
Primary Examiner
August 22, 2005